



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 201 and 207

[Docket No. FDA-2021-N-1351]

RIN 0910-AI52

Revising the National Drug Code Format and Drug Label Barcode Requirements

AGENCY: Food and Drug Administration, Department of Health and Human Services (HHS).

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA, the Agency, or we) is proposing to amend our regulations governing the format of the National Drug Code (NDC). The NDC is an FDA standard for uniquely identifying drug products marketed in the United States. This action, if finalized, will standardize the format of all NDCs. Specifically, all NDCs will be required to be 12 digits in length with 3 distinct segments and 1 uniform format. The first segment is the labeler code and will be 6 digits, the second segment is the product code and will be 4 digits, and the third segment is the package code and will be 2 digits. Additionally, we are proposing to revise the drug product barcode label requirements to permit the use of other data carriers that meet certain standards.

DATES: Either electronic or written comments on the proposed rule must be submitted by **[INSERT DATE 120 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]**. Submit comments on information collection issues under the Paperwork Reduction Act of 1995 (PRA) by **[INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]**.

ADDRESSES: You may submit comments as follows. Please note that late, untimely filed comments will not be considered. The <https://www.regulations.gov> electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of **[INSERT DATE 120 DAYS**

AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are received on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2021-N-1351 for “Revising the National Drug Code Format and Drug Label Requirements.” Received comments, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the

prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

Submit comments on information collection issues under the PRA: Submit comments on the information collection under the PRA to the Office of Management and Budget (OMB) at <https://www.reginfo.gov/public/do/PRAMain>. Find this particular information collection by selecting “Currently under Review--Open for Public Comments” or by using the search function. The title of this proposed collection is “Revising the National Drug Code Format and Drug Label Requirements.”

FOR FURTHER INFORMATION CONTACT: *With regard to the aspects of the proposed rule pertaining to human drug products:* Leyla Rahjou-Esfandiary, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 2262, Silver Spring, MD 20993, 301-796-3185, leyla.rahjou-esfandiary@fda.hhs.gov.

With regard to the aspects of the proposed rule pertaining to human biological drug products: Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993, 240-402-7911, stephen.ripley@fda.hhs.gov.

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SUPPLEMENTARY INFORMATION:

Table of Contents

I. Executive Summary

A. Purpose of the Proposed Rule

B. Summary of the Major Provisions of the Proposed Rule

C. Legal Authority

D. Costs and Benefits

II. Table of Abbreviations/Commonly Used Acronyms in This Document

III. Background

A. Current Regulatory Framework and the Need for the Regulation

B. History of the Rulemaking

IV. Legal Authority

V. Description of the Proposed Rule

A. Adoption of a Uniform 12-Digit NDC

B. Scope/Applicability

C. Implementation of New, Uniform, 12-Digit NDC

D. Proposed Delayed Effective Date

E. Proposed Transition Period

VI. Proposed Effective Date(s)

VII. Preliminary Economic Analysis of Impacts

A. Introduction

B. Summary of Costs and Benefits

VIII. Analysis of Environmental Impact

IX. Paperwork Reduction Act of 1995

X. Federalism

XI. Consultation and Coordination with Indian Tribal Governments

XII. References

I. Executive Summary

A. Purpose of the Proposed Rule

FDA is proposing to modify our regulations to establish a uniform, 12-digit format for the NDC (21 CFR 207.33) that can accommodate longer NDCs once FDA begins issuing 6-digit labeler codes. FDA estimates that it will exhaust its inventory of available 5-digit labeler codes and begin assigning 6-digit labeler codes in 10-15 years. The use of a consistent, uniform format is intended to eliminate the need to convert NDCs from one of FDA's prescribed formats to a different standardized format used by other sectors of the healthcare industry (e.g., healthcare providers and payors). FDA is also proposing to revise the drug barcode label requirements to allow the use of either linear or nonlinear barcodes, so long as the barcode meets the prescribed standards.

B. Summary of the Major Provisions of the Proposed Rule

Under the proposed rule, FDA would amend its regulations to adopt a uniform, 12-digit format for the NDC. As proposed, NDCs will continue to consist of three segments: the labeler code, the product code, and the package code. However, we are proposing that the labeler code be 6 digits, the product code be 4 digits, and the package code be 2 digits. To provide maximum flexibility on the type of barcode used on the label of a drug product, we are proposing to allow the use of either linear or nonlinear barcodes, so long as the barcode meets one of the prescribed standards in § 201.25 (21 CFR 201.25).

On the effective date of the final rule, FDA would begin assigning new NDCs in the uniform, 12-digit format, and existing 10-digit NDCs assigned by FDA prior to the effective date would be required to convert to the new, uniform, 12-digit NDC format. As a result, all stakeholders that use FDA-assigned NDCs would need to have systems capable of handling the new, uniform, 12-digit NDC on the effective date of the final rule. Therefore, FDA is proposing to delay the effective date of the final rule for a period of 5 years following its publication to allow stakeholders time to develop and implement such systems.

Additionally, FDA is proposing to allow for a 3-year transition period following the effective date of the final rule. During this proposed 3-year transition period, firms that use 10-

digit NDCs assigned prior to the effective date on product labeling should begin updating their labeling to replace the 10-digit NDCs with the new 12-digit NDCs by adding leading zeros to the labeler code, product code, and/or package code segments as needed, as soon as possible.

However, to aid with the transition, FDA does not intend to object to continued use of such 10-digit NDCs on the labeling of products remaining in interstate commerce after the effective date during the 3-year transition period. The purpose of the transition period is to mitigate the potential costs associated with reprinting labels for these products. Therefore, during this proposed transition period, stakeholders should ensure that their systems are capable of handling both 10-digit NDCs and 12-digit NDCs.

C. Legal Authority

FDA is proposing to amend our regulations on foreign and domestic establishment registration and listing for drugs, including biological products and animal drugs. FDA's authority for this proposed rule derives from the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 321, *et seq.*) applicable to drugs, including biological products, and the biological product provisions of the Public Health Service Act (PHS Act) (42 U.S.C. 262, *et seq.*). In particular, the proposed rule will standardize the format of NDCs assigned under section 510(e) of the FD&C Act (21 U.S.C. 360(e)) and will aid in efficient enforcement of the FD&C Act pursuant to section 701(a) (21 U.S.C. 371(a)) and section 351(j) of the PHS Act.

D. Costs and Benefits

The proposed rule, if finalized, would require that all NDCs, including any 10-digit NDCs issued by FDA prior to the effective date, be 12 digits in length with a uniform format. Specifically, the NDC will consist of three segments: a 6-digit labeler code, a 4-digit product code, and a 2-digit package code. As a result, product labeling that includes a product's 10-digit NDC would need to be updated to convert the 10-digit NDC to the standard 12-digit format.

One expected benefit of the proposed rule, if finalized, is that the proposed standardized format would facilitate the adoption of a single NDC format by all stakeholders. Such an

adoption would eliminate the need to convert NDCs from one of FDA’s prescribed formats to a different standardized format used by other sectors of the healthcare industry (e.g., healthcare providers and payors). Eliminating the need to convert NDCs should reduce potential errors caused by converting from the FDA-assigned NDC format to a different format used by other sectors of the healthcare industry. Standardization and adoption of a single format would also eliminate the need for additional quality control and validation by certain stakeholders, such as payors and prescribers, to ensure a drug product and its respective NDC are accurate; this is particularly important for insurance coverage and reimbursement claims. Another benefit of the proposed rule would be to avoid any potential risks to the public health from potential reductions in medication errors and risk of confusion. We do not have data to quantify these potential benefits and request comments.

The costs to industry of converting current NDC codes to the proposed format would include one-time costs of updating software systems, new training for employees, coordinating labeling updates, and reading and understanding the proposed rule. Industry, however, can incorporate any changes to existing labeling due to this proposed rule into their recurring labeling updates and avoid any relabeling costs. Some software and training costs would occur even without the proposed rule because FDA will begin issuing 6-digit labeler codes, and the current 10-digit NDC formats are not capable of accommodating 6-digit labeler codes. Our estimates, therefore, are conservative. We estimate annualized costs would be about \$12.4 million ranging from \$6.1 million to \$19.4 million using a 7-percent discount rate over a 10-year horizon. Similarly, we estimate annualized costs would be about \$10.2 million ranging from \$5.1 million to \$16.0 million using a 3-percent discount rate over a 10-year horizon. The present-value of the estimated costs would be \$87.1 million ranging from \$43.1 million to \$136.3 million at both the 7-percent and 3-percent discount rates.

II. Table of Abbreviations/Commonly Used Acronyms in This Document

Abbreviation/Acronym	What It Means
ANDA	Abbreviated New Drug Application
BLA	Biologics License Application

EAN/UCC	European Article Number/Uniform Code Council
FDA	Food and Drug Administration
FD&C Act	Federal Food, Drug, and Cosmetic Act
GTIN-14	Global Trade Identification Number 14
HCT/P	Human Cells, Tissues, and Cellular and Tissue-Based Product
HIBCC	Health Industry Business Communications Council
HHS	Department of Health and Human Services
HIPAA	Health Insurance Portability and Accountability Act
NDA	New Drug Application
NDC	National Drug Code
OMB	Office of Management and Budget
PHS Act	Public Health Service Act
PRA	Paperwork Reduction Act of 1995

III. Background

A. Current Regulatory Framework and the Need for the Regulation

The NDC is an FDA standard for uniquely identifying drugs marketed in the United States. Currently, NDCs assigned by FDA contain 10 digits. As currently described in § 207.33(b) (21 CFR 207.33(b)), NDCs consist of three segments: the labeler code, the product code, and the package code. At some point in the next 10 to 15 years, NDC formatting will need to be updated to accommodate longer NDCs because new labelers are continually entering the U.S. market. In 2016, when FDA published the final rule “Requirements for Foreign and Domestic Establishment Registration and Listing for Human Drugs, Including Drugs That Are Regulated Under a Biologics License Application, and Animal Drugs” (the Registration and Listing Final Rule), the Agency stated that when it runs out of 5-digit labeler codes, it will begin assigning 6-digit labeler codes (81 FR 60169 at 60187, August 31, 2016). As a result, under existing regulations, FDA would add 2 new 11-digit NDC formats (6-3-2 and 6-4-1) to accommodate the longer labeler codes. However, FDA acknowledged that some stakeholders expressed an interest in FDA moving to a single, standard format for NDCs and announced that it planned to initiate a public discussion of future formatting options (See *id.*). FDA initiated the

public discussion by holding a public hearing on November 5, 2018, requesting comments from stakeholders on the impact of the transition to 6-digit labeler codes (83 FR 38666)¹.

Section 510(j) of the FD&C Act requires each person who registers an establishment under section 510(b), (c), (d) or (i) to provide FDA with a current list of all drugs manufactured, prepared, propagated, compounded, or processed by the establishment for commercial distribution. Drug products are identified and listed using the NDC (21 CFR 207.49).

The NDC for each listed drug marketed in the United States is a unique 10-digit,² 3-segment number (§ 207.33(b) (21 CFR 207.33(b))). The 3 segments of the NDC include the labeler code, product code, and package code (id.). The first segment, the labeler code, is a unique 4-, 5-, or (in the future) 6-digit number assigned by FDA that identifies the manufacturer, repacker, relabeler, or private label distributor of the drug (id.). The second segment, the product code, is a 3- or 4-digit number that identifies a specific active ingredient, strength, and dosage form of a drug manufactured, repackaged, relabeled, or distributed by the labeler (id.; § 207.35(b) (21 CFR 207.35(b))). The third segment, the package code, is a 1- or 2-digit number that identifies package sizes and types (§ 207.33(b)). Different package codes differentiate between different quantitative and qualitative attributes of the product packaging (§ 207.35). Both the product and package codes are proposed by persons submitting drug listing information (see § 207.33(d)(1)). The Agency will assign a proposed NDC if it has not been used previously, is not currently in use, and has not been reserved for future assignment to a different drug (§ 207.33(d)(2)). The NDC for a given drug is currently in one of the following configurations (with each number representing the number of digits in that segment): 4-4-2, 5-3-2, or 5-4-1.

According to current regulations, labeler codes may consist of 4, 5, or 6 digits (§ 207.33(b)(1)). Currently, 5-digit labeler codes are being assigned by FDA. A 5-digit labeler code format provides FDA with 90,000 labeler codes that could be assigned to drug

¹ <https://www.regulations.gov/document/FDA-2018-N-2610-0001>

² Under 21 CFR 207.33(b), an NDC must consist of 10 or 11 digits, divided into three segments. This FDA 11-digit NDC refers to the NDC length once the Agency starts assigning 6-digit labeler codes.

manufacturers and private label distributors ranging from 10,000 to 99,999. Based on current assignment rates, FDA anticipates that it will run out of 5-digit labeler codes in approximately 10 to 15 years. At that point in the future, FDA will begin assigning 6-digit labeler codes due to exhaustion of 5-digit labeler codes. Under the current regulations, moving to 6-digit labeler codes will expand the entire NDC to 11 digits and, per regulation, allow for two additional NDC configurations: 6-3-2 and 6-4-1, for a total of 5 possible NDC configurations (including the three 10-digit NDC configurations) (see § 207.33(b)(2)).

The Health Insurance Portability and Accountability Act (HIPAA) (Pub. L. 104-191) contains provisions calling for the administrative simplification “of the national standards for electronic health care transactions and code sets, unique health identifiers, and security”³ and specifically references the NDC. In its implementation of these rules, on August 17, 2000, the Department of Health and Human Services (HHS) published the final rule, “Health Insurance Reform: Standards for Electronic Transactions,” which addressed standards for electronic transactions that established NDCs as the standard medical data code set for reporting drugs and biologics in all standard transactions under HIPAA (65 FR 50312 at 50313). If a HIPAA-covered transaction includes a drug, the NDC is required to be part of the medical code data set (see 45 CFR 162.1002(a)(3)). However, in the preamble to the HIPAA regulations, HHS stated that it was adopting a uniform 11-digit format to conform with customary practice used in computer systems (65 FR 50312 at 50329). The HIPAA standard 11-digit NDC format is standardized such that the labeler code is always 5 digits, the product code is always 4 digits, and the package code always 2 digits. To convert a 10-digit NDC to an 11-digit HIPAA standard NDC, a leading zero is added to the appropriate segment to create the 11-digit configuration as defined above.

³ See <https://www.hhs.gov/ocr/privacy/hipaa/administrative/index.html> (last accessed March 22, 2017).

When FDA moves to a 6-digit labeler code, FDA's new 11-digit native NDC⁴ configurations will have the same number of digits as required by the HIPAA standards, but they will not be in the same format. An 11-digit native NDC will have an extra labeler code digit but will be short a digit in either the product code or package code. Additionally, some of the systems that utilize HIPAA standard 11-digit NDCs⁵ do not use hyphens to separate the segments which, as illustrated below, will result in some 11-digit native NDCs being indistinguishable from HIPAA standard 11-digit NDCs. Therefore, to ensure unhyphenated NDCs are distinguishable, FDA anticipates that the HIPAA standards, and other code sets that currently require 10-digit native NDCs to be converted to 11-digit NDCs, will likely need to be updated in some manner.

Table 1.--NDC Conversion Example

Native NDC Format	Converted NDC Format		
	10-Digit Hyphenated	11-Digit Converted (Hyphenated)	11-Digit Converted (Unhyphenated)
Native 10-digit (5-3-2)	10010-001-01	10010-0001-01	10010000101
Native 11-digit (6-3-2)		100100-001-01	10010000101

FDA is proposing to adopt a single, uniform, 12-digit NDC format to avoid confusion and reduce medication errors that could result, if, as described above, FDA were to begin issuing 11-digit NDCs and the HIPAA standards, and other code sets, that require 10-digit native NDCs to be converted to 11-digit NDCs are not updated. Specifically, standardizing the NDC to one format should eliminate the need for stakeholders to constantly convert a drug's FDA-assigned NDC to a different standardized format because those stakeholders seeking a standardized format will be able to adopt FDA's new, uniform, 12-digit format. This should reduce errors caused by converting from FDA's current nonstandardized NDC format to a standardized format. Additionally, standardization should eliminate the need for stakeholders to use multiple versions of an NDC (e.g., the FDA-assigned 10-digit NDC and the converted HIPAA standard 11-digit NDC).

⁴ NDCs in the format and with the digits assigned by FDA are referred to as *native NDCs*.

⁵ NDCs that contain additional digits necessary to comply with HIPAA standards are referred to as *converted NDCs*.

Finally, using 12-digits will allow FDA to adopt a uniform NDC format without requiring extensive changes to existing 10-digit NDCs. Instead, stakeholders would only need to add leading zeros to certain segments of the existing 10-digit NDC to convert it to the new 12-digit NDC.

B. History of the Rulemaking

1. 2016 Final Rule

In 2016, FDA published the Registration and Listing Final Rule. Recognizing that FDA would run out of 5-digit labeler codes in the near future, the Registration and Listing Final Rule established two additional NDC configurations: 6-3-2 and 6-4-1, for a total of five possible NDC configurations (including the three 10-digit NDC configurations) (§ 207.33(b)(2)). At the same time, FDA acknowledged in the preamble to the Registration and Listing Final Rule that some stakeholders recommended that FDA adopt a single, standard format for NDCs instead and announced that it planned to initiate a public discussion of future formatting options (81 FR 60169 at 60187).

2. 2018 Public Hearing

On November 5, 2018, FDA began these public discussions by holding a public hearing.⁶ At the public hearing, FDA outlined several proposed formatting options that FDA could adopt once it begins issuing 6-digit labeler codes. Specifically, FDA outlined the following four formatting options:

Option A: Do not revise the regulations and continue with the status quo. Under this option, FDA would continue assigning the remainder of the 5-digit labeler codes and whenever the Agency runs out of 5-digit labeler codes, start assigning 6-digit labeler codes. This would expand FDA's NDC inventory to 10 and 11 digits, resulting in 5 different configurations. FDA would use 10- and 11-digit NDCs.

⁶ <https://www.regulations.gov/document/FDA-2018-N-2610-0001>

Option B: Same as Option A except that FDA would stop issuing 5-digit labeler codes and start issuing 6-digit labeler codes on a specified date in the future, before FDA anticipated running out of 5-digit labeler codes. This option was intended to provide more certainty to stakeholders by establishing a designated future date on which they would need to have systems in place to handle 11-digit NDCs in either 6-4-1 or 6-3-2 format.

Option C: Adopt the hyphenated NDC 11-digit format (5-4-2 format) currently used by the payer industry and convert all current 10-digit NDCs to the hyphenated 11-digit format by adding a leading zero to the short segment of the NDC. When the supply of 5-digit labeler codes is exhausted, FDA would begin assigning 6-digit labeler codes for use in 6-3-2 and 6-4-1 formats. Although this would establish a uniform total length for all NDC codes, there would still be multiple formats. Additionally, there is the potential for an 11-digit format with a 6-digit labeler code and an 11-digit format with a 5-digit labeler code to be identical when the hyphens separating the various segments are removed.

Option D: Allow for the harmonization of NDCs between FDA and other stakeholders by adopting 12-digit NDCs in a single, uniform 6-4-2 format. Once FDA starts assigning 6-digit labeler codes, all NDCs (new and existing) would be required to be presented in a 6-4-2 format. Existing NDCs would be converted from their existing format by adding leading zeros to the short segments. This would create one standard configuration for all NDCs that can be used by all stakeholders without conversion. As an added benefit, it would provide the industry with more product or package codes.

An appropriate number of years would be necessary to adapt existing databases and structures to be able to handle the new, uniform, 12-digit NDC and for industry to adopt this as the single NDC format. Therefore, under this option, FDA would implement this change on a prespecified date that would occur before the current pool of 5-digit labeler codes is exhausted, to provide certainty and predictability to industry stakeholders, government payers, and other interested parties.

FDA received oral comments during the hearing, and written comments were submitted afterwards. Most of the comments were in favor of FDA's adoption of a single standardized format that could be used by all stakeholders. The majority of the commenters were also in favor of FDA establishing a certain date when stakeholders would be required to have systems capable of handling the new format, with many advocating for a 10-year delay. For the most part, the commenters were not in favor of options A, B, or C. Instead, in general, the commenters either favored option D, or advocated for FDA to no longer be responsible for assigning NDCs and, instead, allow for a third party to take over that role. FDA considered these comments in developing this proposed rule.

IV. Legal Authority

FDA is proposing to amend our regulations on foreign and domestic establishment registration and listing for drugs, including biological products and animal drugs. FDA's authority for this proposed rule derives from the FD&C Act applicable to drugs, including biological products and the biological product provisions of the PHS Act. In particular, this proposed rule will standardize the format of NDCs assigned under section 510(e) of the FD&C Act and will aid in efficient enforcement of the FD&C Act pursuant to sections 701(a) and 351(j) of the PHS Act.

V. Description of the Proposed Rule

A. Adoption of a Uniform 12-Digit NDC

We are proposing to replace the existing NDC formats with a uniform, 12-digit format (see proposed amendments to § 207.33(b)). Under the proposed rule, the NDC would remain a 3-segment numerical code consisting of the labeler code, the product code, and the package code. However, we are proposing to establish a uniform length for each segment to create a uniform format. Specifically, we are proposing that the labeler code would be 6 digits in length, the product code would be 4 digits in length, and the package code would be 2 digits in length (a 6-4-2 format).

The new format requirements we are proposing would not apply only to NDCs assigned after the effective date of the final rule. Instead, if finalized as proposed, all existing 10-digit NDCs would be converted to the new, uniform, 12-digit format by the addition of leading zeros to the labeler code, the product code, and/or package code segments as needed to produce the 6-4-2 format.

Before deciding to propose the new, uniform, 12-digit NDC, FDA considered not only the four options outlined above, but also several proposals submitted as comments to the public hearing docket. Although many of the comments were supportive of the uniform, 12-digit NDC, others raised concerns that this could impact the ability to use barcodes that utilize GS1's Global Trade Identification Number 14 (GTIN-14) because GTIN-14 is only capable of encoding NDCs up to 10 digits.⁷ Those raising this concern suggested that FDA no longer be responsible for assigning NDCs and, instead, delegate assignment of NDCs to third parties, similar to unique device identifiers. However, we chose not to adopt this alternative because, unlike the implementation of the unique device identifier requirements, FDA is already deeply involved in the assignment of NDCs and changing this system has the potential to cause significant disruption, particularly with the handling of a transition from FDA-assigned NDCs to a new, third-party-assigned NDC. Although there may be some disruption resulting from the implementation of a new, uniform, 12-digit NDC, FDA will be in the best position to minimize and mitigate the disruption because it would continue to be involved in the process for assigning the new 12-digit NDCs. If this responsibility were handed over to a third party, FDA would have less ability to minimize and mitigate the disruption.

One commenter suggested that FDA could retain its 10-digit NDC format after it ran out of the current lot of 5-digit labeler codes by starting to assign 5-digit, alphanumeric labeler codes. Although this would allow firms to continue using their existing 10-digit NDCs, it would not accomplish the goal of uniformity advocated by many commenters. Additionally, except for

⁷ The GTIN-14 is a global numerical data structure containing 14 numbers.

systems used for certain minimally manipulated human cells, tissues, and cellular and tissue-based products (HCT/P) under § 207.33(b)(4), it would not likely relieve many stakeholders of the requirement to update their systems to be capable of handling the new NDC format, as many current systems are unlikely to be able to handle alphanumeric NDCs. Finally, we had some concerns that the introduction of alphabetic characters into the labeler code could increase the risk of medication errors because some may misread a letter as a number. Some examples include similarity between lowercase letter “o” and uppercase letter “O” with numeral 0 (zero), or uppercase letter “B” with numeral 8 (eight).

After taking these and other suggestions into consideration, FDA chose to propose the uniform, 12-digit NDC format because it could be adopted by all stakeholders seeking uniformity and would not require conversion between formats in perpetuity. We recognize that during the transition period described in section V.E. below, there will still need to be some conversion between the existing 10-digit NDC formats and the new, uniform, 12-digit format. However, as noted further below, this would be temporary, and FDA intends to publish, on our website, NDCs in both formats to facilitate these conversions. We also recognize that the establishment of a new, uniform, 12-digit NDC may require changes to other standards in order for stakeholders to adopt the 12-digit NDC as a universal standard. However, it is likely that any change from the 10-digit NDC format would have required such changes, and, as FDA is running out of 5-digit labeler codes, a change is necessary.

B. Scope/Applicability

This proposed rule will affect all drug products that are required to be listed under section 510 of the FD&C Act and 21 CFR part 207. Specifically, once effective, all existing 10-digit NDCs will be required to convert to the new uniform 12-digit NDC format, and all new NDCs will be assigned in the 12-digit format.

However, FDA will still allow the following HCT/Ps, if they are minimally manipulated, to use an alternatively formatted NDC that is approved for use by the relevant Center Director:

Hematopoietic stem/progenitor cells derived from peripheral and cord blood, and lymphocytes collected from peripheral blood (§ 207.33(b)(4)). HCT/Ps that do not fall within the exception set forth in § 207.33(b)(4) would be required to use the new 12-digit NDC format. This proposed rule only relates to FDA's assignment of NDCs; it does not propose any revisions to the HIPAA standard code set.

C. Implementation of New, Uniform, 12-Digit NDC

1. Issuance of New, Uniform, 12-Digit NDCs

On the effective date of the final rule (which we propose would be 5 years from publication of the final rule), FDA would no longer assign 5-digit labeler codes or 10-digit NDCs. Instead, FDA would begin only issuing 6-digit labeler codes and NDCs in the new, uniform, 12-digit format. Therefore, all drug listing files submitted on or after the effective date proposing a new NDC would be required to use the uniform, 12-digit (6-4-2) NDC format. For example, if such a proposal is submitted by a firm with a 4- or 5-digit labeler code, the firm would need to convert its labeler code to a 6-digit labeler code by adding one or two leading zeros, as appropriate, and request the new NDC in the 6-4-2 format. If the submission involves a drug that is being listed for the first time or a change to an already listed drug that requires the use of a new product code under § 207.35(b), the firm must ensure that it is requesting a unique, 12-digit NDC, including a unique, 4-digit product code. If the submission involves a request to assign a new package code for a product already listed with a 10-digit NDC, the firm would need to convert its 4- or 5-digit labeler code to a 6-digit labeler code by adding one or two leading zeros.

If the firm currently uses the 5-3-2 format, it would additionally need to convert the existing product code from a 3-digit code to a 4-digit code by adding a leading zero to achieve the 6-4-2 format. If the firm currently uses the 5-4-1 format, it would not need to convert the existing product code because it is already four digits. However, it still would need to convert its labeler code to six digits and would need to request a unique package code.

As all new NDCs will only be assigned using the new, uniform, 12-digit format starting on the effective date of the final rule, all stakeholders will need to have systems in place that are capable of handling the new, uniform, 12-digit NDCs. However, as described in more detail below in section V.E., during the 3-year transition period, FDA does not intend to object to continued use of 10-digit NDCs assigned prior to the effective date on product labels. Therefore, during this proposed transition period, stakeholders should ensure that their systems are capable of handling both 10-digit and 12-digit NDCs.

2. Converting Existing 10-Digit NDCs

To reduce the burden on registrants, FDA does not intend to require them to resubmit all of their existing drug listing files to convert the NDCs from one of the discontinued 10-digit formats to the new, uniform, 12-digit, 6-4-2 format. Instead, FDA intends to convert existing NDCs on its own, on the effective date, by adding leading zeros to the appropriate segments. Additionally, for the reasons described in more detail below regarding the transition period, FDA intends to begin publishing, on the effective date, both the 10-digit and 12-digit NDCs for those drugs with NDCs assigned prior to the effective date.

3. The Effect on Other Non-FDA NDC Formats

As mentioned above, FDA decided to propose replacing the multiple 10- and possibly 11-digit NDC formats with a new, uniform, 12-digit format, in part, because of concerns that an FDA-assigned 11-digit NDC could be identical to a HIPAA converted 11-digit NDC for a different drug if the hyphens are removed. FDA could have chosen to avoid this by replacing its 11-digit formats with a 12-digit format, while still keeping the 10-digit formats. However, this would still have required an update to the HIPAA standard format so that it could accommodate the new FDA-assigned 12-digit format and likely still would have required at least the FDA-assigned 10-digit NDCs to be converted to a new HIPAA standard format. Although this may have reduced some of the initial burden of converting existing 10-digit NDCs to the new, uniform, 12-digit format, this approach would likely have required stakeholders to update their

systems a second time and would have required ongoing conversion from FDA's NDC formats to the HIPAA standard format(s). Thus, this option would require a conversion and would also create costs, while not reducing the overall risk of medication errors. Therefore, FDA is proposing to adopt a single, uniform, 12-digit NDC format in hopes that it will be adopted as the new HIPAA standard format for NDCs, and no conversions will be necessary from FDA's NDC format to the HIPAA standard format.

In addition to impacting the HIPAA standard format, we recognize that a 12-digit NDC may impact some stakeholders who use the GTIN-14 data standard to encode FDA's 10-digit NDC in the barcode on their label because the GTIN-14 cannot accommodate a 12-digit NDC. We acknowledge that FDA's establishment of a uniform, 12-digit NDC may require the development of new data standard(s) that can enable an NDC of this length to be encoded in a data carrier such as barcodes. That is one of the considerations that went into FDA's proposal to delay the effective date of the final rule, as this would provide time for the development of new data standard(s) and any respective changes to data carriers to accommodate an NDC of this length.

Recognizing that new data standard(s) may be necessary to encode the new, uniform, 12-digit NDC into a data carrier, we propose to revise § 201.25(c) to allow the use of linear or nonlinear barcodes that meet specified standards. FDA is considering whether to further revise § 201.25(c) to accommodate potential advances in technologies and standards development by allowing the use of unspecified automatic identification and data capture formats other than linear or nonlinear barcodes in the future without the need to revise the regulation again. Therefore, we are asking stakeholders to provide comments on whether to include such flexibility.

D. Proposed Delayed Effective Date

We propose to delay the effective date of the final rule for a period of 5 years following its publication. Delaying the effective date of the final rule is intended to provide stakeholders

sufficient time to update their systems to be able to handle the new, uniform 12-digit NDC format, and plan on updating their labeling during the transition period, in a way that reduces burden to them. The delay is also intended to provide sufficient time to implement the necessary corresponding changes to the HIPAA standards and data standards that can enable an NDC of this length to be encoded in a data carrier such as barcodes, as discussed above. FDA is proposing a fixed effective date relative to the publication of the final rule to provide stakeholders with certainty as to when they would need to implement systems capable of handling the new, uniform 12-digit NDC format. However, in establishing the specific effective date, FDA will need to ensure that it occurs before FDA runs out of 5-digit labeler codes. Therefore, this 5-year effective date may result in stakeholders having less time to update their systems to be able to handle the new, uniform 12-digit NDC format than if the effective date were established based on when FDA runs out of 5-digit labeler codes.

The proposed 5-year delay balances the need to give stakeholders sufficient time to update their systems and make other necessary changes to be able to handle the new, uniform 12-digit NDC format, with the need to ensure that the final rule is effective before FDA runs out of 5-digit labeler codes and needs to start issuing 6-digit labeler codes. At this time, FDA believes there are sufficient 5-digit labeler codes remaining such that FDA can delay the effective date of the final rule for a period of 5 years following its publication. However, since the time FDA began developing this proposed rule, the rate at which labeler codes are assigned has increased significantly, particularly due to an influx of requests during the COVID-19 pandemic. Therefore, recognizing the importance of providing certainty to all stakeholders regarding the date on which they will all be expected to have systems in place capable of handling the new 12-digit NDC, FDA intends to reevaluate, prior to publishing the final rule, whether sufficient 5-digit labeler codes remain to allow for a 5-year delay in the effective date. FDA may finalize a shorter delay in the effective date based on our estimation of when we anticipate running out of 5-digit labeler codes. FDA believes this approach to ensuring FDA does not run out of 5-digit

labeler codes before the effective date is a better approach than either of the two following alternatives: (1) accelerating the effective date after publication of the final rule by promulgating a new rule with a shorter effective date or (2) beginning to issue 6-digit labeler codes and 11-digit NDCs before the effective date.

E. Proposed Transition Period

FDA is proposing a 3-year transition period following the effective date of the final rule during which FDA does not intend to object if drugs that were assigned a 10-digit NDC prior to the effective date continue to be labeled with the 10-digit NDC. However, if a firm includes an NDC in its labeling, we would request that the firm start labeling drugs that were assigned a 10-digit NDC with the new 12-digit NDC as soon as possible, but no later than when a firm runs out of its existing labeling inventory for the drug and orders or begins printing new labeling. At the end of the transition period (i.e., 8 years after the publication of the final rule), all firms will be required to use a 12-digit NDC in listing files, and FDA will no longer exercise enforcement discretion with respect to the 12-digit NDC format requirement for all products that include the NDC on their labeling that are introduced or offered for introduction into interstate commerce. As noted above, during this transition period, FDA will continue to maintain and publish 10-digit NDCs for listed drugs, simultaneously with the converted 12-digit NDCs. However, FDA does not intend to continue publishing and maintaining the 10-digit NDCs after the end of this transition period. Therefore, FDA encourages firms to begin labeling these products with the 12-digit NDC as soon as possible after the effective date to ensure that, at the end of the transition period, there are no products labeled with an old, 10-digit NDC remaining in interstate commerce.

FDA is proposing this 3-year transition period to facilitate a smooth transition from the current 10-digit NDC formats to the new, uniform 12-digit NDC format. In light of the nature of the drug supply chain, FDA recognizes that it would be difficult for firms to immediately transition from a 10-digit NDC to a 12-digit NDC without a transition period. Specifically, if on

the effective date, all drugs were required to be labeled with a 12-digit NDC and there was no enforcement discretion regarding 10-digit NDC-labeled products remaining in interstate commerce, then firms would be required to remove products labeled with the 10-digit NDC from interstate commerce and either destroy them or relabel them. As the cost to the firms would be based on the volume of product remaining on the market with the 10-digit NDC, this could incentivize firms to minimize how much product remains on the market at the time of the transition. This could increase the risk of a drug shortage which could harm the public health.

At the same time, the coexistence of drug labeling with either the 10- or 12-digit NDC for a period of time poses its own risks to the public health. Specifically, it raises the risk of confusion, medication errors, and possibly, the risk of the introduction of illegitimate product into the market because of the confusion. In an effort to balance these risks, FDA is proposing to limit the transition period to 3 years following the effective date. FDA is proposing a 3-year transition period for two reasons. First, the expiration date of many drugs is no more than 2 years. Therefore, there should not be many drugs remaining in interstate commerce labeled with NDCs in the 10-digit format at the end of the transition period so long as firms start labeling their products with the 12-digit NDC within the first year after the effective date. Second, most firms make changes to the labeling of a human prescription drugs at least once every 3 years.⁸ Therefore, even if a firm wanted to wait until the next time it implemented a labeling change before transitioning from the 10-digit to a 12-digit NDC, most firms would be able to do so within the transition period.

Additionally, FDA intends to mitigate the risk of medication error and confusion during the transition period by maintaining and publishing both the 10-digit and 12-digit NDC formats for products assigned a 10-digit NDC prior to the effective date. This will provide stakeholders with a resource to confirm the identity of the drug in the event of any confusion.

VI. Proposed Effective Date(s)

⁸ For rates of labeling revisions for prescription drug products, see Ref. 2. For nonprescription products, see Ref. 3.

We are proposing to delay the effective date of the final rule until 5 years after its publication in the *Federal Register*. However, as discussed in section V.D above, FDA may finalize the rule with a shorter effective date to ensure it is effective before FDA runs out of 5-digit labeler codes and is required to start issuing 6-digit labeler codes.

In addition, as discussed in section V.E above, to minimize possible disruption to the distribution of products subject to this proposed rule and to minimize the burden on manufacturers and labelers, FDA is proposing to provide for a 3-year transition period following the effective date. During this transition period, firms with products that were assigned 10-digit NDCs prior to the effective date of the final rule will need to use a 12-digit NDC for all drug listings submitted to FDA and should transition to using a 12-digit NDC on labeling.

VII. Preliminary Economic Analysis of Impacts

A. Introduction

We have examined the impacts of the proposed rule under Executive Order 12866, Executive Order 13563, the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Pub. L. 104-4). Executive Orders 12866 and 13563 direct us to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). We believe that this proposed rule is not a significant regulatory action as defined by Executive Order 12866.

The Regulatory Flexibility Act requires us to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because the one-time cost could be as much as 0.56 percent of average annual revenue for some very small stakeholders in the insurance industry, 0.45 percent of average annual revenue for some very small stakeholders in the pharmaceutical industry, and 0.02 percent of average annual revenue for some very small

stakeholders in the healthcare industry, we propose to certify that the proposed rule, if finalized, would not have a significant economic impact on a substantial number of small entities.

The Unfunded Mandates Reform Act of 1995 (section 202(a)) requires us to prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing “any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any one year.” The current threshold after adjustment for inflation is \$158 million, using the most current (2020) Implicit Price Deflator for the Gross Domestic Product. This proposed rule would not result in an expenditure in any year that meets or exceeds this amount.

B. Summary of Costs and Benefits

This proposed rule, if finalized, would amend regulations governing the format of the NDC by standardizing the format of NDCs to be 12 digits in length. Currently FDA-assigned NDCs are 10-digits and can be in multiple formats. The NDC for each listed drug in the United States is a unique 3-segment number, where the 3 segments are the labeler code, product code, and package code. The proposed standardized NDC would consist of three segments: a 6-digit labeler code, a 4-digit product code, and a 2-digit package code. If the proposed rule is finalized, FDA-assigned 10-digit NDCs would need to be updated to convert to the uniform 12-digit format by adding leading zeros to the respective segments.

One expected benefit of the proposed rule, if finalized, is that the proposed standardized format would facilitate the adoption of a single NDC format by all stakeholders. Such an adoption would eliminate the need to convert NDCs from one of the FDA-prescribed formats to a different standardized format used by other sectors of the healthcare industry (e.g., healthcare providers and payors). Eliminating the need to convert NDCs should reduce potential errors caused by converting from the FDA-assigned NDC format to a different format used by other sectors of the healthcare industry. Standardization and adoption of a single format would also

eliminate the need for additional quality control and validation by certain stakeholders, such as payors and prescribers, to ensure a drug product and its respective NDC are accurate; this is particularly important for insurance coverage and reimbursement claims. Another benefit of the proposed rule would be to avoid any potential risks to the public health from potential reductions in medication errors and risk of confusion. We do not have data to quantify these potential benefits and request comments.

The costs to industry of converting current NDC codes to the proposed format would include one-time costs of updating software systems, new training for employees, coordinating labeling updates, and reading and understanding the proposed rule. Table 2 shows a summary of the quantified costs of the proposed rule. We estimate annualized costs would be about \$12.4 million ranging from \$6.1 million to \$19.4 million using a 7-percent discount rate over a 10-year horizon. Similarly, we estimate annualized costs would be about \$10.2 million ranging from \$5.1 million to \$16.0 million using a 3-percent discount rate over a 10-year horizon. The present-value of the estimated costs would be \$87.1 million ranging from \$43.1 million to \$136.3 million at both the 7-percent and 3-percent discount rates.

Table 2.--Summary of Benefits, Costs, and Distributional Effects of Proposed Rule

Category		Primary Estimate	Low Estimate	High Estimate	Units			Notes
					Year Dollars	Discount Rate	Period Covered	
Benefits	Annualized Monetized millions/year					7%		
						3%		
	Annualized Quantified					7%		
						3%		
	Qualitative	Potential reductions in annual audits, billing issues, cost of software, and medication error.						
Costs	Annualized Monetized millions/year	\$12.4	\$6.1	\$19.4		7%		
		\$10.2	\$5.1	\$16.0		3%		
	Annualized Quantified					7%		
						3%		
	Qualitative							
Transfers	Federal Annualized Monetized millions/year					7%		
						3%		
	From/ To	From:			To:			
	Other Annualized					7%		
						3%		

Category		Primary Estimate	Low Estimate	High Estimate	Units			Notes
					Year Dollars	Discount Rate	Period Covered	
	Monetized millions/year							
	From/To	From:			To:			
Effects	State, Local or Tribal Government: No estimated effect.							
	Small Business: One-time cost could be no more than 0.56 percent of annual revenue for some very small stakeholders with fewer than 5 employees in the insurance industry, 0.45 percent in the pharmaceutical industry, and 0.02 percent also for some very small stakeholders in the healthcare industry.							
	Wages: No estimated effect.							
	Growth: No estimated effect.							

We have developed a comprehensive Preliminary Economic Analysis of Impacts that assesses the impacts of the proposed rule. The full preliminary analysis of economic impacts is available in the docket for this proposed rule (Ref. 4) and at <https://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/EconomicAnalyses/default.htm>.

VIII. Analysis of Environmental Impact

We have determined under 21 CFR 25.30(k) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

IX. Paperwork Reduction Act of 1995

This proposed rule contains information collection provisions that are subject to review by OMB under the PRA (44 U.S.C. 3501-3521). A description of these provisions is given in the *Description* section of this document with an estimate of the recordkeeping burden. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

FDA invites comments on these topics: (1) whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including

through the use of automated collection techniques, when appropriate, and other forms of information technology.

Title: Format of National Drug Code

Description: The proposed rule would require that the respondents identified below revise the format of their NDCs and would require that some of these respondents update any of their product labeling that include the NDC to incorporate the new NDC format. For drugs subject to a new drug application (NDA) or abbreviated new drug application (ANDA), the respondent would be required to report these labeling changes through an annual report; therefore, this proposed rule affects the reporting burden associated with § 314.81(b)(2)(iii) (21 CFR 314.81(b)(2)(iii)). For biological products subject to a biologics license application (BLA), the respondents will be required to report these labeling changes through an annual report; therefore, this proposed rule affects the reporting burden associated with § 601.12(f)(3) (21 CFR 601.12(f)(3)).

Section 314.81(b)(2)(iii) requires the submission of an annual report containing a representative sample of the package labels, currently used professional labeling, patient brochures, package inserts, and a summary of labeling changes (or if no changes have been made, a statement to that effect) since the previous report. Under this proposed rule, the change in the NDC format would result in a labeling change. We have previously estimated the reporting burden for submitting labels as currently required under § 314.81(b)(2)(iii), and OMB has approved the collection of information under OMB control number 0910-0001. We are not re-estimating these approved burdens in this rulemaking. We are only estimating the additional reporting burden associated with the submission of labeling changes associated with the 12-digit NDC format under § 314.81(b)(2)(iii). We have previously estimated the reporting burden for submitting labels as currently required under § 601.12(f)(3), and OMB has approved the collection of information under OMB control number 0910-0338. We are not re-estimating the approved burden in this proposed rule. We are only estimating the additional reporting burden

associated with the submission of labeling changes associated with the 12-digit NDC format under § 601.12(f)(3).

One-time costs and annual operating and maintenance costs associated with the proposed rule are discussed in Section II.F--Costs of the Proposed Rule of the Preliminary Regulatory Impact Analysis (PRIA). However, many of these costs are not associated with the information collections subject to OMB review under the PRA but, instead, are associated with changes in their usual and customary business operations as a result of the new NDC format. Additionally, many of the costs discussed in the PRIA are incurred by firms other than the respondents described below.

To minimize recordkeeping burden that would result from implementing the proposed changes to the NDC format, we provide for 5-year delay in the effective date and a 3-year implementation period. The purpose of this phased-in implementation is to allow respondents to make the labeling change that would result from the proposed change in NDC format at the time of any periodic update that may be made during the 3-year implementation period. Based on the frequency at which drug labeling is updated, we anticipate that nearly all firms will be able to incorporate the labeling change required by this proposed rule as part of a labeling change that they intend to make unrelated to this proposed rule. Therefore, we believe that the incremental information collection burden associated with this proposed rule is likely to be de minimis. However, for purposes of this burden estimate, we have estimated the one-time burden associated with this proposed rule, assuming conservatively that all finished prescription drug products and all finished over-the-counter drug products include the NDC on the label and their label would be updated solely for the purposes of modifying the format of the NDC on their label.

Description of Respondents: Manufacturers, repackers, relabelers, drug product salvagers, and private label distributors are subject to the regulatory requirements in 21 CFR

parts 201 and 207, application holders are subject to the regulatory requirements of § 314.81, and license holders are subject to the regulatory requirements of § 601.12.

We estimate the burden of the information collection as follows:

Table 3.--Estimated One-Time Recordkeeping Burden¹

Format of National Drug Code; Implementing New Requirements	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Section 201.25 (barcode labeling requirements); and part 207, subpart D (requirements for the NDC)	12,800	22.5	288,000	1	288,000
Section 314.81(b)(2)(iii) (other postmarketing reports) or § 601.12(f)(3) (changes to an approved BLA)	2,000	6	12,000	10 minutes (0.167 hours)	2,000

¹Figures have been rounded.

We have characterized the information collection as a recordkeeping burden consistent with 44 U.S.C. 3502(13)(C), which defines the term “recordkeeping requirement” to include records disclosed to third parties, the Federal Government, or the public. Our estimates are based on the following assumptions:

- We assumed that all listed drug packages include the NDC format on their label and that none of the respondents would be able to include these labeling changes into other labeling changes they were making during the transition period. As the change should not require a substantial redesign, but would only require a slight change to the existing NDC format already included on the label, we assumed that each label change would take a respondent 1 hour. Based on the drug listing database, we understand that there are approximately 12,800 respondents and 288,000 listed drug packages, resulting in an estimated burden of 288,000 or 22.5 hours per respondent to change the labels for these products.
- For prescription drugs whose label changes would be reported in an annual report pursuant to § 314.81 or § 601.12(f)(3) for biological products, there are approximately 2,000 respondents that would submit reports and there are approximately 12,000 active approved applications. This means that on average each application holder will need to

submit 6 annual reports (12,000 active approved applications \times 1 annual report per active approved application/2000 unique application holders). Information on listed drugs indicates there are approximately 120,000 separate, identifiable product packages that that are subject to an approved ANDA, BLA, or NDA. This means that on average each separate and distinct approved application includes approximately 10 separate and distinct product packages (120,000 unique distinct product packages/12,000 unique approved applications). Section 314.81(b)(2)(iii) requires firms to submit an annual report that includes a summary of any changes in labeling since the last annual report. Similarly, § 601.12(f)(3)(i)(A) requires manufacturers of biologics to include in their annual reports editorial or similar minor labeling changes. We expect that the updating of the NDC format on a label would necessitate a simple statement in the annual report declaring that the NDC format has been updated, so we have assigned an estimate of 1 minute for such statements per label. As each annual report will include 10 such declarations (one for each unique product package), we estimate the burden to report these changes to be approximately 10 minutes per annual report. Thus, the total reporting burden would be 2,000 hours (2,000 respondents \times 6 annual reports per respondent \times 10 minutes per annual report/60 minutes = 2,000 hours).

To ensure that comments on information collection are received, OMB recommends that written comments be submitted through <https://www.reginfo.gov> (see ADDRESSES). All comments should be identified with the title of the information collection.

In compliance with the Paperwork Reduction Act of 1995 (44 U.S.C. 3507(d)), we have submitted the information collection provisions of this proposed rule to OMB for review. These information collection requirements will not be effective until FDA publishes a final rule, OMB approves the information collection requirements, and the rule goes into effect. FDA will announce OMB approval of these requirements in the *Federal Register*.

X. Federalism

We have analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132. We have determined that this proposed rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, we conclude that the rule does not contain policies that have federalism implications as defined in the Executive Order and, consequently, a federalism summary impact statement is not required.

XI. Consultation and Coordination With Indian Tribal Governments

We have analyzed this proposed rule in accordance with the principles set forth in Executive Order 13175. We have tentatively determined that the proposed rule does not contain policies that would have a substantial direct effect on one or more Indian Tribes, on the relationship between the Federal Government and Indian Tribes, or on the distribution of power and responsibilities between the Federal Government and Indian Tribes. The Agency solicits comments from tribal officials on any potential impact on Indian Tribes from this proposed action.

XII. References

The following references are on display at the Dockets Management Staff (see ADDRESSES) and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they are also available electronically at <https://www.regulations.gov>. FDA has verified the website addresses, as of the date this document publishes in the *Federal Register*, but websites are subject to change over time.

1. HIPAA for Professionals, available at <https://www.hhs.gov/ocr/privacy/hipaa/administrative/index.html> (last accessed March 22, 2021).
2. Eastern Research Group, Inc. (2003), “The Pharmaceutical Labeling Revisions Cost Model,” January 2, 2003, Contract No. 223-94-8031, Task Order No. 8.

3. RTI International (2015), “2014 FDA Labeling Cost Model.”

4. FDA, Preliminary Regulatory Impact Analysis, “Format of National Drug Code,”

available at

<https://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/EconomicAnalyses/default.htm>.

List of Subjects

21 CFR Part 201

Drugs, Labeling, Reporting and recordkeeping requirements.

21 CFR Part 207

Drugs, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, and under authority delegated to the Commissioner of Food and Drugs, the Food and Drug Administration proposes to amend 21 CFR parts 201 and 207 as follows:

PART 201—LABELING

1. The authority citation for part 201 is revised to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 358, 360, 360b, 360gg-360ss, 371, 374, 379e; 42 U.S.C. 216, 241, 262, 264.

2. In § 201.25:

- a. Revise the section heading;
- b. Remove the word “bar code” and add the word “barcode” in its place; and
- c. Revise paragraph (c)(1) introductory text.

The revisions read as follows:

§ 201.25 Barcode label requirements.

* * * * *

(c) * * *

(1) Each drug product described in paragraph (b) of this section must have a barcode that contains, at a minimum, the appropriate National Drug Code (NDC) number in a linear or

nonlinear format approved by the relevant Food and Drug Administration Center Director.

Approved standards include those that meet European Article Number/Uniform Code Council (EAN/UCC) or Health Industry Business Communications Council (HIBCC) standards.

Additionally, the barcode must:

* * * * *

**PART 207—REQUIREMENTS FOR FOREIGN AND DOMESTIC ESTABLISHMENT
REGISTRATION AND LISTING FOR HUMAN DRUGS, INCLUDING DRUGS THAT
ARE REGULATED UNDER A BIOLOGICS LICENSE APPLICATION, AND ANIMAL
DRUGS, AND THE NATIONAL DRUG CODE**

3. The authority citation for part 207 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 355, 360, 360b, 371, 374, 381, 393; 42 U.S.C.
262, 264, 271.

4. In § 207.33, revise paragraph (b) to read as follows:

**§ 207.33 What is the National Drug Code (NDC), how is it assigned, and what are its
requirements?**

* * * * *

(b) *What is the format of an NDC?* (1) Except as described in paragraph (b)(2) of this section, the NDC must consist of 12 digits, divided into three segments as follows:

(i) The first segment of the NDC is the labeler code and consists of 6 digits. The labeler code is assigned by FDA.

(ii) The second segment of the NDC is the product code and consists of 4 digits.

(iii) The third segment of the NDC is the package code and consists of 2 digits. The package code identifies the package size and type of the drug and differentiates between different quantitative and qualitative attributes of the product packaging.

(2) An alternatively formatted NDC that is approved for use by the relevant Center Director may be used for the following HCT/Ps if they are minimally manipulated:

Hematopoietic stem/progenitor cells derived from peripheral and cord blood, and lymphocytes collected from peripheral blood.

* * * * *

Dated: July 11, 2022.

Robert M. Califf,

Commissioner of Food and Drugs.

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